OCT 2 6 2006 PARADEMARKO

SEQUENCE LISTING

<110> Protein Design Labs, Inc. Ramakrishnan, Vanitha Powers, David Johnson, Dale E Jeffry, Ursula Bhaskar, Vinay <120> Chimeric and Humanized Antibodies to alpha5betal Integrin That Modulate Angiogenesis <130> 05882.0178.NPUS01 <140> 10/724,274 <141> 2003-11-26 <150> 60/429,743 <151> 2002-11-26 60/508,149 <150> <151> 2003-09-30 <160> 47 <170> PatentIn version 3.2 <210> <211> 124 <212> PRT <213> mus musculus <400> Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
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35 40 45
Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys 50 60
Ser Arg Met Thr Ile Ser Lys Asp Asn Ser Lys Ser Thr Val Tyr Leu 65 70 75 80
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Tyr Cys Ala
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Page 2

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Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys 50 55 60
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Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Met Thr Ile Ser Lys Asp Asn Ser Lys Ser Thr Val Tyr Leu 65 70 75 80

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Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ala Pro Asn Leu Trp 35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser 50 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu 65 70 75 80

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Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Trp 35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser 50 55 60

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Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp 35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser 50 55 60

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Met Gln 65 70 75 80

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Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu 35 40 45

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln 65 70 75 80

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Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp 35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Vål Pro Ser Arg Phe Ser Page 7

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Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp 35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser 50 60

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln 70 75 80

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Page 8

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Ser Ala Pro Asn Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly 65 70 75 80
Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
85 90 95
Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His 100 \hspace{1cm} 105 \hspace{1cm} 110
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Thr Asp Tyr Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu 50 60
Glu Trp Leu Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser 65 70 75 80
Ala Leu Lys Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln
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Val Phe Leu Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr
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Artificial Sequence

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Met Ser Ala Ser Leu Gly Glu Arg Val Thr Met Thr Cys Thr Ala Ser 40 45

Ser Ser Val Ser Ser Asn Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly 50 60

Ser Ala Pro Asn Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly 70 75 80

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu $85 \hspace{1cm} 90 \hspace{1cm} 95$

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His $100 \hspace{1cm} 105 \hspace{1cm} 110$

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                                                                     180
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                                                                     960
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                                                                    1080
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                                                                    1200
                                                                    1260
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Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu 35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln Val Phe Leu 65 70 75 80

Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr Tyr Cys Ala 85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Gly Asp Ala Leu Asp 100 105 110

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu 130 135 140 Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro 145 150 155 160 Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr 165 170 175 Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val 180 185 190 Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn 195 200 205 Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser 210 220 Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly 225 230 235 240 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln 260 265 270 Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr 290 295 300 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 305 310 315 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile 325 330 335 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350 Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser 355 360 365 . Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val 405 410 415

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445

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Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu 65 70 75 80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro 85 90 95

Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala 100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser 115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Page 17 Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser 145 150 155 160 Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu 165 170 175 Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val 180 185 190 Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys 195 200 205 Ser Phe Asn Arg Gly Glu Cys <210> 27 696 Artificial Sequence <220> <223> chimeric antibody <400> 27 60 caggtgcagc tgaaggagtc aggacctggc ctggtggcgc cctcacagag cctgtccatc 120 acatgcacca tctcagggtt ctcattaacc gactatggtg ttcactgggt tcgccagcct 180 ccaggaaagg gtctggagtg gctggtagtg atttggagtg atggaagctc aacctataat 240 tcagctctca aatccagaat gaccatcagg aaggacaact ccaagagcca agttttctta 300 ataatgaaca gtctccaaac tgatgactca gccatgtact actgtgccag acatggaact tactacggaa tgactacgac gggggatgct ttggactact ggggtcaagg aacctcagtc 360 420 accgtctcct cagcttccac caagggccca tccgtcttcc ccctggcgcc ctgctccagg 480 agcacctccg agagcacagc cgccctgggc tgcctggtca aggactactt ccccgaaccg 540 gtgacggtgt cgtggaactc aggcgccctg accagcggcg tgcacacctt cccggctgtc ctacagtcct caggactcta ctccctcagc agcgtggtga ccgtgccctc cagcagcttg 600

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Ser Leu Ser Ile Thr Cys Thr Ile Ser Gly Phe Ser Leu Thr Asp Tyr 20 25 30

Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu 35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys 50 60

Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln Val Phe Leu 65 70 75 80

Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr Tyr Cys Ala 85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys 115 120 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu 130 135 140

Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro 145 150 155 160

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr 165 170 175

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val 180 185 190

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn 195 200 205

Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser 210 215 220

Lys Tyr Gly Pro Pro Cys Pro Ser 225 230

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                                                                      360
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ccatctgatg	agcagttgaa	atctggaact	gcctctgttg	tgtgcctgct	gaataacttc	420
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Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu 35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys 50 55 60

Ser Arg Met Thr Ile Ser Lys Asp Asn Ala Lys Asn Thr Val Tyr Leu 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

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Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val 405 410 415

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445

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<223> chimeric antibody

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Glu Arg Ala Thr Leu Ser Cys Thr Ala Ser Ser Ser Val Ser Ser Asn $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu 35 40

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser 50 60

Gly Ser Gly Ser Gly Thr Ser Tyr Thr Leu Thr Ile Ser Ser Leu Glu 65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro 85 90 95

Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala 100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser 115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Page 23

130

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                                                                         48
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<211> 143
<212> PRT
<213> mus musculus
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Met Ala Val Leu Gly Leu Leu Leu Cys Leu Val Thr Phe Pro Ser Cys 1 5 10 15
Val Leu Ser Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala 20 25 30
                                    Page 26
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Pro Ser Gln Ser Leu Ser Ile Thr Cys Thr Ile Ser Gly Phe Ser Leu 35 40 45

Thr Asp Tyr Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu 50 60

Glu Trp Leu Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser 70 75 80

Ala Leu Lys Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln 85 90 95

Val Phe Leu Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr 100 105 110

Tyr Cys Ala Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Gly Asp $115 \hspace{1.5cm} 120 \hspace{1.5cm} 125$

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Val Ile Met Ser Arg Gly Gln Ile Val Leu Thr Gln Ser Pro Ala Ile 20 25 30

Met Ser Ala Ser Leu Gly Glu Arg Val Thr Met Thr Cys Thr Ala Ser 40 45

Ser Ser Val Ser Ser Asn Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly 50 55 60

Ser Ala Pro Asn Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly 70 75 80

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu 85 90 95

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His
100 105 110
Page 27